Point of Contact:
Jan Delaval
Librarian-Physical Sciences
CM1 1E01 Tel: 308-4498

```
$%^STN;HighlightOn=;HighlightOff=;
=> fil reg
FILE 'REGISTRY' ENTERED AT 11:38:48 ON 18 SEP 2001
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STRUCTURE FILE UPDATES:   17 SEP 2001  HIGHEST RN 357258-84-5
DICTIONARY FILE UPDATES:  17 SEP 2001  HIGHEST RN 357258-84-5

TSCA INFORMATION NOW CURRENT THROUGH January 11, 2001

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Structure search limits have been increased.  See HELP SLIMIT
for details.

=> d sta que l2
L1          118 SEA FILE=REGISTRY ABB=ON  PLU=ON  GPETLCGAELVDALQFVCGDRGF.FNKPT
                G.GSSSRRAPQTGIVDECC...C.L..LEM.CAPLKPAKSA/SQSP
L2           42 SEA FILE=REGISTRY ABB=ON  PLU=ON  L1 AND 70/SQL


=> d his

     (FILE 'HOME' ENTERED AT 10:25:50 ON 18 SEP 2001)
                SET COST OFF

     FILE 'REGISTRY' ENTERED AT 10:25:59 ON 18 SEP 2001
L1          118 S GPETLCGAELVDALQFVCGDRGF.FNKPTG.GSSSRRAPQTGIVDECC...C.L..LEM.C
                SAV L1 MOEZIE399/A
L2           42 S L1 AND 70/SQL
                E INSULIN-LIKE GROWTH FACTOR/CN
L3            1 S E1
L4            1 S E6
L5            1 S E11
L6            1 S E26
L7           42 S L2 NOT L3-L6
L8            3 S L3-L6
                E INSULIN-LIKE GROWTH FACTOR I (HUMAN)/CN
L9            1 S E3
                E INSULIN-LIKE GROWTH FACTOR (HUMAN)/CN
                E INSULIN-LIKE GROWTH FACTOR II (HUMAN)/CN
L10           1 S E3
L11           5 S L8-L10
L12           4 S L11 NOT L7

     FILE 'HCAPLUS' ENTERED AT 10:32:27 ON 18 SEP 2001
L13         162 S L7
L14       16081 S L12
L15       16437 S (IGF OR INSULIN LIKE GROWTH FACTOR OR INSULIN GROWTH FACTOR O
L16       20977 S IGF OR INSULIN LIKE GROWTH FACTOR OR INSULIN GROWTH FACTOR OR
L17        1737 S IGF1 OR IGF2
L18         467 S INSULINLIKE GROWTH FACTOR()(1 OR I OR 2 OR II)
L19        2656 S INSULINLIKE GROWTH FACTOR
L20        5078 S (IGF OR INSULIN LIKE GROWTH FACTOR OR INSULIN GROWTH FACTOR O
L21         763 S SOMATOMEDIN# C
L22         870 S IGFI OR IGFII
L23       21794 S L14-L22
L24         140 S L13 AND (PD<=19981002 OR PRD<=19981002 OR AD<=19981002 OR PY<
L25       16524 S L23 AND (PD<=19981002 OR PRD<=19981002 OR AD<=19981002 OR PY<
                E MASCARENHAS D/AU
L26          42 S E3-E6,E10
L27           2 S L26 AND L13
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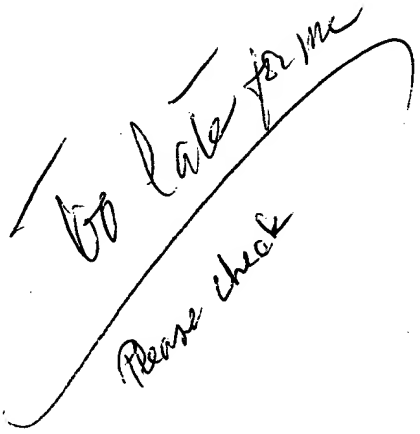

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L28          19 S L26 AND L23
L29           2 S L27 AND L25
L30           2 S L27,L29
L31          23 S L7 (L) THU/RL
L32          17 S L31 AND L24
L33          18 S L24 AND (?NEOPLAS? OR ?TUMOR? OR ?TUMOUR? OR ?MALIGNA? OR ?CA
                E CANCER/CT
                E E3+ALL
                E E2+ALL
L34      193090 S E3-E8,E2+NT
                E E132+ALL
L35       77037 S E4
L36       52430 S E3,E21-E66
                E E68+ALL
L37        3932 S E4,E3
                E HYBRIDOMA/CT
                E E3+ALL
L38        4007 S E6,E5+NT
L39           5 S L24 AND L34-L38
L40          18 S L33,L39
L41           3 S L31 AND L40
L42           5 S L7(L) BAC/RL AND L40
L43           7 S L30,L41,L42
L44           7 S L43 AND L13-L42
                SEL DN 3 6 7
L45           4 S L44 NOT E1-E3
L46        1197 S L25 AND L34-L38
L47        4721 S L25 AND (?NEOPLAS? OR ?TUMOR? OR ?TUMOUR? OR ?MALIGNA? OR ?CA
L48        1109 S L12 (L) THU/RL
L49        4359 S L12 (L) BAC/RL
L50        1129 S L46,L47 AND L48,L49
L51         203 S L12 (L) THU/RL AND L50
L52          18 S L51 AND (ANTITUMOR AGENT OR REDUCE C JUN EXPRESSION OR CACHEX
L53          21 S L45,L52
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 11:34:15 ON 18 SEP 2001
L54           5 S E4-E8

     FILE 'HCAPLUS' ENTERED AT 11:34:31 ON 18 SEP 2001
L55          34 S L31-L33 NOT L53
L56           5 S L55 AND (SYRUP OR BLAST OR MYOBLAST)

     FILE 'REGISTRY' ENTERED AT 11:38:48 ON 18 SEP 2001

=> d sqide can tot l54

L54 ANSWER 1 OF 5  REGISTRY  COPYRIGHT 2001 ACS
RN   151913-90-5  REGISTRY
CN   Insulin-like growth factor I (human reduced), 60-L-leucine- (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   1: PN: WO0020023 FIGURE: 1 claimed protein
CN   insulin-like growth factor I [60-leucine] (human)
FS   PROTEIN SEQUENCE
SQL  70

SEQ      1 GPETLCGAEL VDALQFVCGD RGFYFNKPTG YGSSSRRAPQ TGIVDECCFR
        51 SCDLRRLEML CAPLKPAKSA
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, TOXLIT
                1 REFERENCES IN FILE CA (1967 TO DATE)
                1 REFERENCES IN FILE CAPLUS (1967 TO DATE)
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REFERENCE 1: 132:246740

L54 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN **68562-41-4** REGISTRY
CN Insulin-like growth factor I (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN CEP 151
CN FK 780
CN GroPep
CN Human IGF-I
CN Human insulin-like growth factor I
CN Human insulin-like growth factor-I, isomer II
CN Human somatomedin C
CN Insulin-like growth factor 1 (pig)
CN Mecasermin
CN Myotrophin
FS PROTEIN SEQUENCE
SQL 70
NTE

type	------ location ------		description
bridge	Cys-6	- Cys-48	disulfide bridge
bridge	Cys-18	- Cys-61	disulfide bridge
bridge	Cys-47	- Cys-52	disulfide bridge

SEQ 1 GPETLCGAEL VDALQFVCGD RGFYFNKPTG YGSSSRRAPQ TGIVDECCFR
51 SCDLRRLEMY CAPLKPAKSA
DR 155924-93-9
MF C331 H512 N94 O101 S7
CI MAN
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAPLUS, CBNB, CIN, CSCHEM, DRUGNL, DRUGPAT, DRUGUPDATES, IPA, MEDLINE, MRCK*, PROMT, RTECS*, TOXLINE, TOXLIT, USAN, USPATFULL
(*File contains numerically searchable property data)
99 REFERENCES IN FILE CA (1967 TO DATE)
9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
99 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:279086

REFERENCE 2: 134:141889

REFERENCE 3: 133:350495

REFERENCE 4: 133:155311

REFERENCE 5: 133:100059

REFERENCE 6: 133:100050

REFERENCE 7: 132:246741

REFERENCE 8: 132:203275

REFERENCE 9: 132:45102

REFERENCE 10: 131:154015

L54 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN **67763-97-7** REGISTRY
CN Insulin-like growth factor II (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Growth factors (animal), multiplication-stimulating activity, III-2

CN IGF 2
CN IGF-II
CN Insulin-like growth factor 2
CN Multiplication-stimulating activity III-2
MF Unspecified
CI PMS, MAN
PCT Manual registration
LC STN Files: AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
3859 REFERENCES IN FILE CA (1967 TO DATE)
70 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3864 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:178662

REFERENCE 2: 135:178660

REFERENCE 3: 135:178258

REFERENCE 4: 135:175747

REFERENCE 5: 135:175437

REFERENCE 6: 135:165265

REFERENCE 7: 135:163261

REFERENCE 8: 135:162974

REFERENCE 9: 135:162181

REFERENCE 10: 135:147768

L54 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN **67763-96-6** REGISTRY
CN Insulin-like growth factor I (9CI) (CA INDEX NAME)
OTHER NAMES:
CN IGF-1
CN IGF-I
CN Insulin-like growth factor 1
CN insulin-like growth factor I
CN Somatomedin 1
CN Somatomedin C
CN Sulfation factor C
DR 61461-67-4
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CBNB, CEN, CHEMCATS, CIN, CSCHEM, DDFU, DRUGU, EMBASE, MEDLINE, MRCK*, PHAR, PROMT, RTECS*, TOXLINE, TOXLIT, USPATFULL, VETU
(*File contains numerically searchable property data)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
13054 REFERENCES IN FILE CA (1967 TO DATE)
257 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
13074 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:179713

REFERENCE 2: 135:179088

REFERENCE 3: 135:179068

REFERENCE 4: 135:178918

REFERENCE 5: 135:178917

REFERENCE 6: 135:178881

REFERENCE 7: 135:178869

REFERENCE 8: 135:178855

REFERENCE 9: 135:178845

REFERENCE 10: 135:178808

L54 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2001 ACS
RN **61912-98-9** REGISTRY
CN Insulin-like growth factor (9CI) (CA INDEX NAME)
OTHER NAMES:
CN IGF
CN Insulin, -like activity
CN Insulin-like activity, nonsuppressible
CN Nonsuppressible insulin-like activity
CN Nonsuppressible insulin-like growth factor
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: ADISNEWS, AGRICOLA, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CEN, CHEMCATS, CIN, EMBASE, PROMT, TOXLINE, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
1786 REFERENCES IN FILE CA (1967 TO DATE)
58 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1788 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:185454

REFERENCE 2: 135:175437

REFERENCE 3: 135:170830

REFERENCE 4: 135:170786

REFERENCE 5: 135:165492

REFERENCE 6: 135:164785

REFERENCE 7: 135:163359

REFERENCE 8: 135:157731

REFERENCE 9: 135:147768

REFERENCE 10: 135:147539

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 11:39:23 ON 18 SEP 2001
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FILE COVERS 1947 - 18 Sep 2001 VOL 135 ISS 13
FILE LAST UPDATED: 17 Sep 2001 (20010917/ED)

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=> d all tot l53

L53 ANSWER 1 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:240980 HCAPLUS
DN 132:246741
TI Methods for the treatment of non-thyroid disorders using **IGF**, IGFBP, and thyroid axis agonists or antagonists
IN **Mascarenhas, Desmond**
PA Celtrix Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-30
ICS A61K031-4164; A61K031-505; A61P035-00; A61P025-00; A61P011-00; A61P013-00; A61K038-30; A61K038-17
CC 2-10 (Mammalian Hormones)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020024	A2	20000413	WO 1999-US22761	19990929 <--
	WO 2000020024	A3	20000706		
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9964070	A1	20000426	AU 1999-64070	19990929 <--
	EP 1117425	A2	20010725	EP 1999-951681	19990929 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	US 1998-102790	P	19981002 <--		
	US 1999-399134	A	19990920		
	WO 1999-US22761	W	19990929		

AB Methods are disclosed for the treatment of non-thyroid disorders which respond to **IGF**, respond to IGFBP-3, or which are **IGF**-dependent. Thyroid axis agonists and **IGF** are administered to subjects suffering from non-thyroid disorders which respond to **IGF**, alleviating the symptoms of the disorders. Thyroid axis antagonists and IGFBP-3 are administered to subjects suffering from non-thyroid disorders which respond to IGFBP-3, alleviating the symptoms of the disorders. Thyroid axis antagonists are administered to subjects suffering from **IGF**-dependent non-thyroid disorders, thereby alleviating the symptoms of the disorders.
ST nonthyroid disorder treatment **IGF** IGFBP thyroid axis modulator
IT **Insulin-like growth factor**-binding proteins

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGF**-BP-3, complex with **IGF-I**; methods for treatment of non-thyroid disorders using **IGF**, IGFBP, and thyroid axis agonists or antagonists)

IT **Insulin-like growth factor**-binding proteins
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**IGF**-BP-3; methods for treatment of non-thyroid disorders using **IGF**, IGFBP, and thyroid axis agonists or antagonists)

IT Thyroid hormones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; methods for treatment of non-thyroid disorders using **IGF**, IGFBP, and thyroid axis agonists or antagonists)

IT Thyroid hormones
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for treatment of non-thyroid disorders using **IGF**, IGFBP, and thyroid axis agonists or antagonists)

IT Thyroid hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods for treatment of non-thyroid disorders using **IGF**, IGFBP, and thyroid axis agonists or antagonists)

IT Disease, animal
(non-thyroid disorders; methods for treatment of non-thyroid disorders using **IGF**, IGFBP, and thyroid axis agonists or antagonists)

IT 51-48-9, L-Thyroxine, biological studies 51-52-5, Propylthiouracil 60-56-0, Methimazole 6893-02-3, Triiodothyronine 9002-71-5, TSH 22232-54-8, Carbimazole 24305-27-9, Thyroid releasing hormone 24305-27-9D, TRH, analogs **61912-98-9**, **IGF** **67763-96-6**, **IGF-I** **67763-96-6D**, **IGF-I**, mutants and complexes with IGFBP-3 **68562-41-4**, Human **IGF-I** **68562-41-4D**, Human **IGF-I**, mutants and complexes with IGFBP-3 130302-14-6, Glycoprotein **IGF**-BP 3 (human clone LCP2.3 subunit protein moiety reduced) 130302-14-6D, Glycoprotein **IGF**-BP 3 (human clone LCP2.3 subunit protein moiety reduced), complexes with **IGF-I**
RL: BAC (Biological activity or effector, except adverse); **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(methods for treatment of non-thyroid disorders using **IGF**, IGFBP, and thyroid axis agonists or antagonists)

L53 ANSWER 2 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:240978 HCAPLUS
DN 132:246740
TI **Null IGF** for the treatment of **cancer**
IN **Mascarenhas, Desmond**
PA Celtrix Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K038-30
ICS A61P035-00; A61K038-30; A61K031-505
CC 2-10 (Mammalian Hormones)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000020023	A2	20000413	WO 1999-US22681	19990929 <--
	WO 2000020023	A3	20000706		
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9962778	A1	20000426	AU 1999-62778	19990929 <--

EP 1117424 A2 20010725 EP 1999-950037 19990929 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRAI US 1998-102747 P 19981002 <--
US 1999-399120 A 19990920
WO 1999-US22681 W 19990929
AB New methods for the treatment of **cancer** are provided. Null **IGF** (**IGF** variants with reduced receptor binding) is administered to subjects having **cancer**, thereby alleviating the symptoms of the **cancer**. The **cancer** to be treated is either breast **cancer**, prostate **cancer**, colon **cancer**, or lung **cancer**. The null **IGF** can be administered with a thyroid axis antagonist (propylthiouracil, methimazole, carbimazole).
ST null **IGF cancer** treatment
IT Thyroid hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(antagonists; null **IGF** for treatment of **cancer** in combination with a thyroid axis antagonist)
IT Intestine, **neoplasm**
(colon, inhibitors; null **IGF** for treatment of **cancer**)
IT **Antitumor agents**
(colon; null **IGF** for treatment of **cancer**)
IT Lung, **neoplasm**
(inhibitors; null **IGF** for treatment of **cancer**)
IT Thyroid hormones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitors; null **IGF** for treatment of **cancer** in combination with a thyroid axis antagonist)
IT **Antitumor agents**
(lung; null **IGF** for treatment of **cancer**)
IT **Antitumor agents**
(mammary gland; null **IGF** for treatment of **cancer**)
IT Mammary gland
Prostate gland
(**neoplasm**, inhibitors; null **IGF** for treatment of **cancer**)
IT **Antitumor agents**
(null **IGF** for treatment of **cancer**)
IT **Antitumor agents**
(prostate gland; null **IGF** for treatment of **cancer**)
IT **61912-98-9D, IGF**, variant **67763-96-6D, IGF-1**, variant **151913-90-5**
RL: **BAC (Biological activity or effector, except adverse)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(null **IGF** for treatment of **cancer**)
IT 51-52-5, Propylthiouracil 60-56-0, Methimazole 22232-54-8, Carbimazole
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(null **IGF** for treatment of **cancer** in combination with a thyroid axis antagonist)

L53 ANSWER 3 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:207256 HCAPLUS
DN 133:99183
TI Use of the **IGF-I antisense** strategy in the treatment of the **hepatocarcinoma**
AU Upegui-Gonzalez, Lia C.; Duc, Huynh T.; Buisson, Yves; Arborio, Michel; Lafarge-Frayssinet, Christiane; Jasmin, Claude; Guo, Yajun; Trojan, Jerzy
CS Hopital Paul Brousse and CNRS Universite Paris XI, Villejuif, 94800, Fr.
SO Adv. Exp. Med. Biol. (**1998**), 451(Gene Therapy of Cancer), 35-42
CODEN: AEMBAP; ISSN: 0065-2598
PB Plenum Press
DT Journal
LA English

CC 1-6 (Pharmacology)
Section cross-reference(s): 2, 15
AB A way to treat **hepatocarcinoma** by inhibition of **IGF-I** factor is proposed. Injection of transfected **hepatoma** cells expressing **IGF-I** antisense could be an effective vaccine against **hepatoma**.
ST **hepatoma antitumor IGFI** antisense vaccine
IT Liver, **neoplasm**
(**hepatoma**, inhibitors; use of the **IGF-I** antisense strategy in the treatment of the **hepatocarcinoma**)
IT **Antitumor agents**
(**hepatoma**; use of the **IGF-I** antisense strategy in the treatment of the **hepatocarcinoma**)
IT Vaccines
(**tumor**; use of the **IGF-I** antisense strategy in the treatment of the **hepatocarcinoma**)
IT Antisense DNA
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of the **IGF-I** antisense strategy in the treatment of the **hepatocarcinoma**)
IT **Antitumor agents**
(vaccines; use of the **IGF-I** antisense strategy in the treatment of the **hepatocarcinoma**)
IT **67763-96-6, IGF-I**
RL: **BAC (Biological activity or effector, except adverse)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(inhibitors; use of the **IGF-I** antisense strategy in the treatment of the **hepatocarcinoma**)
RE.CNT 20
RE
(1) Arbuthnot, P; Hepatology 1995, V22(6), P1788 HCAPLUS
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(8) Hilliard, C; Int J Biochem Cell Biol 1996, V28(6), P639 HCAPLUS
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(15) Trojan, J; Neuroscience Letters 1996, V212, P9 HCAPLUS
(16) Trojan, J; Proc Natl Acad Sci U S A 1992, V89, P4874 HCAPLUS
(17) Trojan, J; Proc Natl Acad Sci U S A 1994, V91, P6088 HCAPLUS
(18) Tu, G; J Biol Chem 1995, V270(47), P28402 HCAPLUS
(19) Venook, A; J Clin Oncol 1994, V12, P1323 MEDLINE
(20) Wanebo, H; CANCER: principles and Practice of Oncology (3 edn) 1989, P836

L53 ANSWER 4 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 2000:207255 HCAPLUS
DN 133:320082
TI Ex vivo and in vivo **IGF-I antisense** RNA strategies for treatment of **cancer** in humans
AU Anthony, D. D.; Pan, Y. X.; Wu, S. G.; Shen, F.; Guo, Y. J.
CS Department of Pharmacology, Case Western Reserve University, Cleveland, OH, 44106, USA
SO Adv. Exp. Med. Biol. (**1998**), 451(Gene Therapy of Cancer), 27-34
CODEN: AEMBAP; ISSN: 0065-2598
PB Plenum Press
DT Journal
LA English

CC 13-5 (Mammalian Biochemistry)
AB The applicability and use was studied of gene therapy methods against **cancer** using an **insulin-like growth factor I** antisense RNA strategy ex vivo and in vivo. The in vivo strategy was economical and expedient but involved invasive procedures eventually leading to complications. With the ex vivo approach transfection frequency could be more readily assessed and the immunogen mechanisms more readily examd. The authors suggest that both approaches will play a role in development of gene therapy programs.
ST gene therapy **anticancer IGFI** antisense RNA
IT **Antitumor agents**
Gene therapy
(**IGF-I** antisense RNA strategies for treatment of **cancer**)
IT Antisense RNA
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**IGF-I** antisense RNA strategies for treatment of **cancer**)
IT **67763-96-6, IGF-I**
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(**IGF-I** antisense RNA strategies for treatment of **cancer**)
RE.CNT 16
RE
(1) D'Ercole, A; Endocrinology and Metabolism Clinics of North America 1996, V25(3), P573 HCAPLUS
(2) Kaleko, M; Mol Cell Biol 1990, V10, P464 HCAPLUS
(3) Kiess, W; Hormone Research 1994, V41(Suppl 2), P66
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L53 ANSWER 5 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:614132 HCAPLUS
DN 131:253353
TI **Tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of **lung cancer**
IN Reed, Steven G.; Wang, Tongtong
PA Corixa Corporation, USA
SO PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12N015-12
ICS A61K038-17; C07K014-47; C07K016-18; A61K035-14
CC 3-3 (Biochemical Genetics)
Section cross-reference(s): 1, 6, 14
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 9947674 A2 19990923 WO 1999-US5798 19990317 <--
WO 9947674 A3 20000120
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
US 6210883 B1 20010403 US 1998-40984 19980318 <--
AU 9930949 A1 19991011 AU 1999-30949 19990317 <--
BR 9908823 A 20001121 BR 1999-8823 19990317 <--
EP 1064372 A2 20010103 EP 1999-912607 19990317 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
NO 2000004631 A 20001115 NO 2000-4631 20000915 <--
PRAI US 1998-40802 A 19980318 <--
US 1998-40984 A 19980318 <--
US 1998-123912 A 19980727 <--
US 1998-123933 A 19980727 <--
WO 1999-US5798 W 19990317

AB Compds. and methods for the treatment and diagnosis of lung **cancer** are provided. The inventive compds. include polypeptides contg. at least a portion of a lung **tumor** protein. Thus, 70 cDNA sequences were isolated from a human lung squamous cell **carcinoma** cDNA expression library and **tumor**-specific polypeptide-encoding cDNAs identified by subtraction with normal lung cDNA libraries and a cDNA library from normal liver and heart; an addnl. 16 cDNA clones were identified from a lung **adenocarcinoma** library. Vaccines and pharmaceutical compns. for immunotherapy of lung **cancer** comprising such polypeptides, or DNA mols. encoding such polypeptides, are also provided, together with DNA mols. for prepg. the inventive polypeptides.

ST **tumor** antigen cDNA lung **cancer** human; vaccine immunotherapy lung **cancer** reagent

IT Connexins
RL: BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(26; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Keratins
RL: BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(6; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Lung, **neoplasm**
(**adenocarcinoma**; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Immunostimulants
(adjuvants; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Diagnosis
(**cancer**; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Escherichia coli
Yeast
(expression host; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Molecular cloning
(expression systems; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Proteins, specific or class

RL: BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(gene NMB; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Lung, **neoplasm**
(inhibitors; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT **Antitumor agents**
(lung; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Animal cell
(mammalian, expression host; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Antibodies
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Proteins, specific or class
RL: BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(plakophilin 1; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Lung, **neoplasm**
(squamous cell **carcinoma**; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Antigen-presenting cell
CD4-positive T cell
CD8-positive T cell
Dendritic cell
Macrophage
T cell (lymphocyte)
(treatment with **proliferated**; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Antigens
RL: BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(**tumor**-assocd.; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Lung, **neoplasm**
PCR (polymerase chain reaction)
Protein sequences
Vaccines
cDNA sequences
(**tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Antibodies
Primers (nucleic acid)
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT Fusion proteins (chimeric proteins)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT 112024-77-8, Humoral hypercalcemic factor (human clone BRF.61 precursor) 160478-25-1 244614-96-8 244615-06-3 244776-64-5 244776-67-8 244776-68-9 244776-71-4 244776-73-6 245058-16-6 245058-17-7 245058-19-9
RL: BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)

(amino acid sequence; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT 9028-31-3, Aldose reductase 103370-86-1, Parathyroid hormone-related peptide
RL: BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(homolog; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT 244259-49-2 244259-76-5 244259-77-6 244259-78-7 244259-79-8
244259-80-1 244259-81-2 244259-82-3 244259-83-4 244259-84-5
244259-85-6 244259-86-7 244259-87-8 244259-88-9 244259-89-0
244259-96-9 244259-97-0 244259-98-1 244259-99-2 244260-00-2
244260-01-3 244260-02-4 244260-03-5 244260-04-6 244260-05-7
244260-06-8 244260-07-9 244260-08-0 244260-09-1 244260-10-4
244260-11-5 244260-13-7 244260-14-8 244260-15-9 244260-18-2
244260-19-3 244260-20-6 244260-21-7 244260-22-8 244260-23-9
244260-24-0 244260-25-1 244260-26-2 244260-27-3 244260-28-4
244609-06-1 244609-07-2 244609-08-3 244609-09-4 244609-10-7
244609-11-8 244609-12-9 244609-13-0 244609-14-1 244609-15-2
244609-16-3 244609-17-4 244609-18-5 244609-19-6 244609-20-9
244609-21-0 244609-22-1 244609-25-4 244609-34-5 244609-35-6
244609-36-7 244609-37-8 244609-38-9 244609-39-0 244609-40-3
244609-41-4 244609-42-5 244609-43-6 244609-44-7 244609-45-8
244609-46-9 244609-47-0 244609-48-1 244609-49-2 244609-50-5
244609-51-6 244609-52-7 244609-53-8 244609-54-9 244609-55-0
244609-56-1 244609-57-2 244609-58-3 244609-59-4 244609-60-7
244609-61-8 244609-62-9 244609-63-0 244609-64-1 244609-65-2
244609-66-3 244609-67-4 244609-68-5 244609-69-6 244609-70-9
244609-71-0 244609-72-1 244609-73-2 244609-74-3 244609-77-6
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244775-06-2 244775-07-3 244775-08-4 244775-09-5 244775-10-8
244775-11-9 244775-12-0 244775-13-1 244776-54-3 244776-55-4
244776-56-5 244776-57-6 244776-58-7 244776-59-8 244776-60-1
244776-61-2 244776-62-3 244776-63-4 244776-65-6 244776-66-7
244776-69-0 244776-70-3 244776-72-5 244776-74-7 244776-75-8
245058-13-3 245058-14-4 245058-15-5 245058-18-8
RL: BOC (Biological occurrence); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(nucleotide sequence; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

IT **61912-98-9, Insulin-like growth factor**
RL: BOC (Biological occurrence); PRP (Properties); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(.beta.2; **tumor**-specific polypeptide-encoding nucleic acids and methods for therapy and diagnosis of lung **cancer**)

L53 ANSWER 6 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:169585 HCAPLUS
DN 131:3463
TI **Insulin-like growth factors** in human **breast cancer**
AU Ellis, Matthew J.; Jenkins, Sara; Hanfelt, John; Redington, Maura E.; Taylor, Marian; Leek, Russel; Siddle, Ken; Harris, Adrian
CS Lombardi Cancer Center, Georgetown University, Washington, DE, 20007, USA
SO Breast Cancer Res. Treat. (**1998**), 52(1-3), 265-274
CODEN: BCTRD6; ISSN: 0167-6806
PB Kluwer Academic Publishers
DT Journal; General Review
LA English

CC 14-0 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2

AB A review, with 62 refs. **IGF1** and **IGF2** are circulating peptide hormones and locally-acting growth factors with both paracrine and autocrine functions. **IGF1** and **IGF2** signal through a common tyrosine kinase receptor, the **insulin-like growth factor 1** receptor (IGF1R), and have mitogenic, cell survival, and insulin-like actions that are essential for embryogenesis, post-natal growth physiol., and breast development. The activities of **IGF1** and 2 are tightly-regulated by a network of binding proteins and targeted degrdn. mechanisms. This complex regulatory system is disrupted in breast **cancer**, leading to excess IGF1R signaling. Evidence for this statement includes: a) breast **cancers** are infiltrated with **IGF2** expressing stromal cells; b) mannose 6-phosphate/**IGF2** receptor (M6P/IGF2R) is mutated in breast **cancer**, leading to loss of **IGF2** degrdn.; c) IGF1R is overexpressed by **malignant** breast epithelial cells, and in some cases IGF1R is amplified; and d) complex changes in **IGF** binding protein expression occur during breast **cancer** progression which most likely also affect **IGF1** and 2 signaling. The clin. importance of these epigenetic and genetic changes has recently been stressed by the finding that IGF1R signaling alters the apoptotic response of breast **cancer** cells to genotoxic stress and, in addn., IGF1R activation sensitizes cells to estrogen by inducing phosphorylation of the estrogen receptor. As a consequence of these findings, we propose that **IGF** anal. of breast **cancer** samples should shift from prognostic studies to an evaluation of **IGF** ligands, receptors, and binding proteins as resistance/sensitivity markers for radiation, **chemotherapy**, and endocrine therapy.

ST review **IGF** breast **cancer**

IT Apoptosis
Biomarkers (biological responses)
Chemotherapy
Prognosis
Radiotherapy
Signal transduction, biological
Tumor markers
(**insulin-like growth factor** system in human breast **cancer**)

IT Estrogen receptors
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(**insulin-like growth factor** system in human breast **cancer**)

IT **Insulin-like growth factor** **I** receptors
Insulin-like growth factor **II** receptors
Insulin-like growth factor-binding proteins
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(**insulin-like growth factor** system in human breast **cancer**)

IT Estrogens
RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BIOL (Biological study); PROC (Process)
(**insulin-like growth factor** system in human breast **cancer**)

IT Mammary gland
(**neoplasm; insulin-like growth factor** system in human breast **cancer**)

IT **67763-96-6, IGF1 67763-97-7, IGF2**

RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)
(**insulin-like growth factor** system in human breast **cancer**)

RE.CNT 62

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L53 ANSWER 7 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1999:20491 HCAPLUS
DN 130:246427
TI Responsiveness to hormone, growth factor and drug treatment of a human **breast cancer** cell line: comparison between early and late cultures
AU De Cupis, Alessandra; Pirani, Paolo; Fazzuoli, Laura; Favoni, Roberto E.
CS Department of Preclinical Oncology, National Institute for Cancer Research, University of Genoa, Genoa, 10-16132, Italy
SO In Vitro Cell. Dev. Biol.: Anim. (**1998**), 34(10), 836-843
CODEN: IVCAED; ISSN: 1071-2690
PB Society for In Vitro Biology
DT Journal
LA English
CC 1-6 (Pharmacology)
Section cross-reference(s): 2
AB Growth rate, morphol., and responsiveness to mitogenic stimuli and pharmacol. treatments were evaluated in early and late cell passages derived from the same clone of the widely used MCF-7 human breast **adenocarcinoma** cell line. The results indicate dissimilarities between early (E) and late (L) passages for some of the parameters analyzed. The cells that underwent many subcultivations grew faster than the others; both appeared homogeneous in size and shape. The E cells, subcultured for almost 1 yr, displayed higher sensitivity to the mitogenic action of both estradiol, according to the level of estrogen receptor, and **insulin-like growth factor-I** than did the L cells, kept in culture for more than 10 yr. Cell responsiveness to two drugs, a novel steroid antiestrogen and a polysulfonated distamycin A deriv., was more pronounced in the early cultures only at the longer time of exposure to the higher concn. of the estrogen antagonist. In addn., a drug-induced inhibition of **insulin-like growth factor-I** binding to its receptor was shown in both E and L cells, the latter being less sensitive than the former when exposed to the antiestrogen. Finally, MCF-7 E and L cells showed similar behavior when drug-induced apoptosis was tested.
ST breast **cancer** inhibitor responsiveness culture age; hormone breast **cancer** inhibitor culture age; growth factor breast **cancer** inhibitor culture
IT Apoptosis
Breast tumor inhibitors
Mammalian tissue culture
(responsiveness to hormone and growth factor and drug treatment of a human breast **cancer** cell line and comparison between early and late cultures in relation to apoptosis induction)
IT 154788-16-6, PNU 145156E
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(PNU 145156E; responsiveness to hormone and growth factor and drug treatment of a human breast **cancer** cell line and comparison between early and late cultures in relation to apoptosis induction)
IT 50-28-2, 17.beta.-Estradiol, biological studies **67763-96-6, Insulin-like growth factor I** 129453-61-8, ICI 182780
RL: **BAC (Biological activity or effector, except adverse); THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(responsiveness to hormone and growth factor and drug treatment of a human breast **cancer** cell line and comparison between early and late cultures in relation to apoptosis induction)
RE.CNT 32
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L53 ANSWER 8 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:544085 HCAPLUS
DN 129:254261
TI New approaches to treatment of **androgen**-independent prostate **cancer** based on peptide analogs
AU Schally, A. V.
CS Endocrine, Polypeptide and Cancer Institute, VA Medical Center and Section of Experimental Med., Dep. Med., Tulane Univ. Sch. Med., New Orleans, LA, USA
SO Curr. Adv. Androl., Proc. Int. Congr. Androl., 6th (**1997**), 81-87. Editor(s): Waites, Geoffrey M. H.; Frick, Julian; Baker, Gordon W. H. Publisher: Monduzzi Editore, Bologna, Italy.
CODEN: 66MSAS
DT Conference; General Review
LA English
CC 1-0 (Pharmacology)
Section cross-reference(s): 2
AB A review with 15 refs. New hormonal methods for treatments of advanced prostate **carcinoma** are being developed based on peptide analogs such as antagonists of LH-releasing hormone (LH-RH), analogs of somatostatin, antagonists of growth hormone-releasing hormone (GH-RH) and antagonists of bombesin/gastrin releasing peptide (GRP). These analogs inhibit **tumor** growth by interfering with the secretion or the receptors of growth factors including epidermal growth factor (EGF), **insulin-like growth factor-I** (**IGF-I**) and bombesin/GRP, which may play a role in the progression and the relapse of prostate **cancer**. A new class of **antitumor** agents based on LH-RH analogs linked to Doxorubicin and its 2-pyrrolino-deriv., which is 500-1000 times more active, is used for targeted **chemotherapy** of prostate **cancer** to produce a local **tumoricidal** effect. Exptl. results with the analogs in nude mice bearing transplanted human prostate **cancer** lines and Dunning rat **tumor** models are summarized as well as clin. findings in patients with advanced prostate **cancer**. Continued

investigation should lead to a more effective therapy for relapsed, androgen-independent prostate **cancer**.

ST review peptide analogs prostate **cancer** inhibition

IT Prostatic **carcinoma**
(androgen-independent; new approaches to treatment of androgen-independent prostate **cancer** based on peptide analogs)

IT **Prostatic tumor inhibitors**
(new approaches to treatment of androgen-independent prostate **cancer** based on peptide analogs)

IT 9002-72-6, Somatotropin 9034-40-6, Luteinizing hormone-releasing factor 51110-01-1, Somatostatin 62229-50-9, Epidermal growth factor **67763-97-7, Insulin-like growth factor II** 160361-88-6
RL: **BAC (Biological activity or effector, except adverse)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(new approaches to treatment of androgen-independent prostate **cancer** based on peptide analogs)

L53 ANSWER 9 OF 21 HCAPLUS COPYRIGHT 2001 ACS

AN 1998:417929 HCAPLUS

DN 129:187556

TI **Insulin-like growth factor 1** and prostate **cancer** risk: a **population**-based, case-control study

AU Wolk, Alicja; Mantzoros, Christos S.; Andersson, Swen-Olof; Bergstrom, Reinhold; Signorello, Lisa B.; Lagiou, Pagona; Adami, Hans-Olov; Trichopoulos, Dimitrios

CS Department of Medical Epidemiology, Karolinska Institutet, Stockholm, S-171 77, Swed.

SO J. Natl. Cancer Inst. (**1998**), 90(12), 911-915
CODEN: JNCIEQ; ISSN: 0027-8874

PB Oxford University Press

DT Journal

LA English

CC 14-1 (Mammalian Pathological Biochemistry)
Section cross-reference(s): 2

AB Recent epidemiol. investigations have suggested an assocn. between increased blood levels of **insulin-like growth factor 1** (**IGF-1**) and increased risk of prostate **cancer**. The authors' goal was to det. whether an assocn. exists between serum levels of **IGF-1** and one of its binding proteins, **insulin-like growth factor**-binding protein 3 (IGFBP-3), and prostate **cancer** risk. An immuno-radiometric assay was used to quantify **IGF-1** levels and IGFBP-3 levels in serum samples as part of a population-based, case-control study in Sweden. The study population comprised 210 patients with newly diagnosed, untreated prostate **cancer** and 224 frequency-matched control subjects. Data were analyzed by use of unconditional logistic regression to calc. odds ratios (ORs) and 95% confidence intervals (CIs). Reported P values are two-sided. The mean serum **IGF-1** level for case patients (158.4 ng/mL) was significantly higher than that for control subjects (147.4 ng/mL); corresponding mean serum IGFBP-3 levels were not significantly different between case patients (2668 ng/mL) and control subjects (2518 ng/mL). The authors found a moderately strong and statistically significant pos. assocn. between serum levels of **IGF-1** levels and risk of prostate **cancer** (OR = 1.51; 95% CI = 1.0-2.26 per 100 ng/mL increment); the assocn. was particularly strong for men younger than 70 yr of age (OR = 2.93; 95% CI = 1.43-5.97). No assocn. was found between serum **IGF-1** levels and disease stage. Serum IGFBP-3 levels were not significantly assocd. with increased risk of disease, and adjustment for IGFBP-3 had little effect on the assocn. between **IGF-1** levels and risk of prostate **cancer**. Elevated serum **IGF-1** levels may be an important predictor of risk for prostate **cancer**. However, the

authors' results do not support an important role for serum IGFBP-3 as a predictor of risk for this disease.
ST **IGF1** prostate **cancer** risk; **insulin like growth factor 1 cancer**
IT Prostatic **tumors**
Risk assessment
Serum (blood)
(serum **insulin-like growth factor 1** and human prostate **cancer** risk)
IT Aging (animal)
(serum **insulin-like growth factor 1** and human prostate **cancer** risk in relation to)
IT **Insulin-like growth factor**-binding protein 3
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(serum **insulin-like growth factor 1** and human prostate **cancer** risk in relation to)
IT **67763-96-6, Insulin-like growth factor I**
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); **THU (Therapeutic use)**; BIOL (Biological study); OCCU (Occurrence); USES (Uses)
(serum **insulin-like growth factor 1** and human prostate **cancer** risk)

L53 ANSWER 10 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:205905 HCAPLUS
DN 128:266320
TI **Insulin-like growth factor-I: clinical studies**
AU Vos, Pieter E.; Koppeschaar, Hans P. F.; De Vries, Wouter R.; Wokke, John H. J.
CS Department of Neurology, University Hospital Utrecht, Utrecht University, Utrecht, Neth.
SO Drugs Today (**1998**), 34(1), 79-90
CODEN: MDACAP; ISSN: 0025-7656
PB J. R. Prous, S.A.
DT Journal; General Review
LA English
CC 2-0 (Mammalian Hormones)
Section cross-reference(s): 1
AB A review with 89 refs. **Insulin-like growth factor-1** (**IGF-I**) has endocrine, autocrine and paracrine properties. Receptors for **IGF-I** are present on virtually all cell types but are located mainly on cells of mesenchymal origin, such as fibroblasts, chondrocytes and osteoblasts. Growth hormone (GH)-dependent and GH-independent actions of **IGF-I** have been implicated in normal and abnormal bone growth, diabetes mellitus, malnutrition, **cancer**, thyroid disease and hematol. diseases. The availability of recombinant human **IGF-I** (rhIGF-I) has led to new treatments for GH-resistant Laron dwarfism and certain diseases assocd. with severe insulin resistance. **IGF-I** has recently been investigated as a neurotrophic factor. Phase II efficacy trials with patients with neurol. disease such as traumatic brain injury, myotonic dystrophy and amyotrophic lateral sclerosis have shown that rhIGF-I has efficacy on various outcome parameters. Treatment with rhIGF-I may result in reversible side effects of which increased heart rate, papilledema, opthalmol. and intracranial hypertension, facial and generalized edema, and wt. gain are noteworthy.
ST review **insulin like growth factor I; IGF I** review
IT **67763-96-6, Insulin-like growth factor-I**
RL: ADV (Adverse effect, including toxicity); **BAC (Biological activity or effector, except adverse)**; **THU (Therapeutic use)**

; BIOL (Biological study); USES (Uses)
(**Insulin-like growth factor-I** therapeutic applications in humans)

L53 ANSWER 11 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1998:124030 HCAPLUS
DN 128:201361
TI **Hematopoietic stem cell proliferating** agents
IN Saito, Yoshimasa; Ueda, Yoshiko; Tamura, Kouichi; Takada, Yoko; Yamada, Choji; Yamashita, Tatsuo; Kobayashi, Masakazu
PA Fujisawa Pharmaceutical Co., Ltd., Japan; Saito, Yoshimasa; Ueda, Yoshiko; Tamura, Kouichi; Takada, Yoko; Yamada, Choji; Yamashita, Tatsuo; Kobayashi, Masakazu
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM A61K038-30
ICS A61K038-17
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 15
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9806422	A1	19980219	WO 1997-JP2818	19970812 <--
	W: JP, US				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 953354	A1	19991103	EP 1997-934775	19970812 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
PRAI	JP 1996-213641		19960813 <--		
	JP 1997-11054		19970124 <--		
	WO 1997-JP2818		19970812 <--		

AB Provided are hematopoietic stem cell **proliferating** agents contg. **IGF-I**, optionally together with at least one protein selected from among SCF, M-CSF and G-CSF; and a process for **proliferating** hematopoietic stem cells characterized by culturing the cells in a medium contg. **IGF-I** and at least one protein selected between M-CSF and SCF. Because of the capability of **proliferating** hematopoietic stem cells in a undifferentiated state either in vivo or in vitro, these agents are usable in the amelioration of cytopenia accompanying radiation therapy or induced by **chemotherapeutics** such as **carcinostatic** agents, the prevention of infectious diseases caused by lymphocytopenia, the culture and **proliferation** of hematopoietic stem cells in vitro, the culture of recombinant stem cells in vitro in gene therapy, etc.
ST hematopoietic stem cell **proliferating** agent **IGF1**
IT Blood cell diseases
(cytopenia; hematopoietic stem cell **proliferating** agents comprises **IGF-1** and at least one of SCF, M-CSF, and G-CSF)
IT **Chemotherapy**
Gene therapy
Hematopoietic stem cell
Infection
Radiotherapy
(hematopoietic stem cell **proliferating** agents comprises **IGF-1** and at least one of SCF, M-CSF, and G-CSF)
IT Stem cell factor
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hematopoietic stem cell **proliferating** agents comprises **IGF-1** and at least one of SCF, M-CSF, and G-CSF)
IT Albumins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(human; hematopoietic stem cell **proliferating** agents

comprises **IGF-1** and at least one of SCF, M-CSF, and G-CSF)

IT Lymphocyte diseases
(lymphocytopenia; hematopoietic stem cell **proliferating** agents comprises **IGF-1** and at least one of SCF, M-CSF, and G-CSF)

IT **Antitumor agents**
(treatment; hematopoietic stem cell **proliferating** agents comprises **IGF-1** and at least one of SCF, M-CSF, and G-CSF)

IT **67763-96-6, IGF-1** 81627-83-0, M-CSF
143011-72-7, G-CSF
RL: **BAC (Biological activity or effector, except adverse)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(hematopoietic stem cell **proliferating** agents comprises **IGF-1** and at least one of SCF, M-CSF, and G-CSF)

L53 ANSWER 12 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:515681 HCAPLUS
DN 127:200136
TI Physical mapping of human **insulin-like growth factor-I** using specific monoclonal antibodies
AU Manes, S.; Kremer, L.; Vangbo, B.; Lopez, A.; Gomez-Mouton, C.; Peiro, E.; Albar, J. P.; Mendel-Hartvig, I. B.; Llopis, R.; Martinez-A, C.
CS Department Immunology Oncology, Centro Nacional Biotecnologia, CSIC, Universidad Autonoma Madrid, Madrid, E-28049, Spain
SO J. Endocrinol. (**1997**), 154(2), 293-302
CODEN: JOENAK; ISSN: 0022-0795
PB Journal of Endocrinology
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
Section cross-reference(s): 15
AB The primary structure of recombinant human (h) **insulin-like growth factor-I** (**IGF-I**) epitopes recognized by a panel of 28 monoclonal antibodies (mAbs) is characterized. Pairwise mAb epitope mapping defines eight 'epitopic clusters' (I-VIII) which cover nearly the entire solvent-exposed **IGF-I** surface. Monoclonal antibody reactivity with 32 overlapping synthetic peptides and with **IGF-I** mutants is used to assoc. these epitopic clusters with the probable primary **IGF-I** sequences recognized. Epitopic cluster I involves residues in the C-domain and the first .alpha.-helix of the A-domain; clusters II, V and VII involve principally the B-domain; clusters III and IV map to amino acid sequences (55-70) and (1-13) resp.; cluster VI includes the A- and B-domains; and cluster VII involves mainly the C-terminal part of the B-domain. Data indicate that this mAb panel defines 14 distinct **IGF-I** epitopes. The specific inhibition of HEL 92.1.7 **IGF-I**-promoted **proliferation** by these mAbs was explored. Direct correlation between mAb affinity and inhibitory activity was obsd. except in the case of clusters III- and VII-specific mAbs. Finally, the combination of epitopic cluster I and II mAbs detect 0.cntdot.5-10 ng/mL hIGF-I in a sandwich immunoassay, with no **IGF-II** cross-reactivity. These anti-**IGF-I** mAbs are, therefore, useful for both the inhibition of **IGF-I** mitogenic activity and for the quantification of this growth factor. The potential use of this mAb panel in **tumor** cell growth control is discussed.
ST epitope mapping **IGF I** monoclonal antibody
IT Cell **proliferation**
Epitope mapping
Protein motifs
.alpha.-Helix (protein conformation)
(human **IGF-I** phys. mapping using specific monoclonal antibodies)
IT Monoclonal antibodies

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(human **IGF-I** phys. mapping using specific monoclonal antibodies)

IT **67763-96-6, IGF-I 68562-41-4,** Human **insulin-like growth factor-I**
RL: ANT (Analyte); **BAC (Biological activity or effector, except adverse)**; PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(human **IGF-I** phys. mapping using specific monoclonal antibodies)

L53 ANSWER 13 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:430115 HCAPLUS
DN 127:131473
TI **Insulin-like growth factor 1 (IGF-1)** alters drug sensitivity of HBL100 human **breast cancer** cells by inhibition of apoptosis induced by diverse **anticancer** drugs
AU Dunn, Sandra E.; Hardman, Rebecca A.; Kari, Frank W.; Barrett, J. Carl
CS Laboratory Molecular Carcinogenesis, National Institute Environmental Health Sciences, Research Triangel Park, NC, 27709, USA
SO Cancer Res. (**1997**), 57(13), 2687-2693
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 1
AB In this study, we tested the hypothesis that **insulin-like growth factor-1 (IGF-1)** modulates apoptosis in human breast **cancer** cells, HBL100, induced by diverse **chemotherapeutic** drugs. **IGF-1** increased cell survival of HBL100 cells treated with 5-fluorouracil (antimetabolite), methotrexate (antimetabolite), tamoxifen (antiestrogen/**antiproliferative**), or camptothecin (topoisomerase 1 inhibitor) and after serum withdrawal. Elevated cell survival was not due to an increase in cell **proliferation** by **IGF-1**, but rather to an inhibition of apoptosis. Evidence for death by apoptosis was supported by cellular morphol. and DNA fragmentation. There were no changes obsd. in Bcl-2 protein or bax mRNA levels. Extracellular matrix (ECM) is known to influence the apoptotic response of cells; therefore, the antiapoptotic effect of **IGF-1** on breast **cancer** cells was examd. using different ECMs: laminin, collagen IV, or Matrigel. **IGF-1** protected cells from apoptosis induced by methotrexate on all ECMs tested, providing the first evidence that **IGF-1** protects against apoptosis in three-dimensional culture systems. These data provide the rationale to search for drugs that lower serum **IGF-1** in an effort to improve the efficacy of **chemotherapeutic** drugs for the treatment of breast **cancer**.
ST **IGF** breast **cancer** apoptosis **anticancer** drug
IT Animal cell line
(HBL100; **IGF-1** alters drug sensitivity of HBL100 human breast **cancer** cells by inhibition of apoptosis induced by diverse **anticancer** drugs)
IT **Antitumor agents**
Apoptosis
Breast tumor inhibitors
Breast **tumors**
Extracellular matrix
Serum (blood)
(**IGF-1** alters drug sensitivity of HBL100 human breast **cancer** cells by inhibition of apoptosis induced by diverse **anticancer** drugs)
IT Laminins

Type IV collagen
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**IGF-1** alters drug sensitivity of HBL100 human breast **cancer** cells by inhibition of apoptosis induced by diverse **anticancer** drugs)

IT 51-21-8, 5-Fluorouracil 59-05-2, Methotrexate 7689-03-4, Camptothecin 10540-29-1, Tamoxifen
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(**IGF-1** alters drug sensitivity of HBL100 human breast **cancer** cells by inhibition of apoptosis induced by diverse **anticancer** drugs)

IT **67763-96-6, IGF-1**
RL: **BAC (Biological activity or effector, except adverse)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**IGF-1** alters drug sensitivity of HBL100 human breast **cancer** cells by inhibition of apoptosis induced by diverse **anticancer** drugs)

IT 119978-18-6, Matrigel
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**IGF-1** alters drug sensitivity of HBL100 human breast **cancer** cells by inhibition of apoptosis induced by diverse **anticancer** drugs)

L53 ANSWER 14 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:343594 HCAPLUS
DN 127:12808
TI **Insulin-like growth factors** and cytokines in **pediatric cancer**
AU Helman, Lee J.; Wexler, Leonard H.
CS Pediatric Branch, National Cancer Institute, USA
SO Growth Factors Cytokines Health Dis. (**1997**), Volume 3B, 331-354.
Editor(s): LeRoith, Derek; Bondy, Carolyn. Publisher: JAI Press, Greenwich, Conn.
CODEN: 64HGAL
DT Conference; General Review
LA English
CC 1-0 (Pharmacology)
Section cross-reference(s): 15
AB A review with 78 refs. The development of clin. applications for hematopoietic growth factors, differentiation and anti-**proliferative** factors, and immunoregulatory cytokines is still in its formative stages in the area of pediatric oncol. The relative rarity of pediatric **cancers** makes it difficult for large-scale studies of these new agents to be conducted. However, smaller pilot studies have been performed and offer clues as to their eventual clin. utility. This chapter will focus on those agents that have been most extensively evaluated in children with **cancer** and will discuss recent lab. insights into basic mechanisms of **tumorigenesis** that offer intriguing new strategies for clin. investigation.
ST **Insulin like growth factor antitumor** review; cytokine **cancer** children **antitumor** review
IT **Antitumor agents**
Child
(**insulin-like growth factors** and cytokines in pediatric **cancer**)
IT Cytokines
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**insulin-like growth factors** and cytokines in pediatric **cancer**)
IT **61912-98-9, Insulin-like growth**

factor
RL: **BAC (Biological activity or effector, except adverse)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**insulin-like growth factors**
and cytokines in pediatric **cancer**)

L53 ANSWER 15 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:44641 HCAPLUS
DN 126:55338
TI **IGF-1** superagonists
IN Dimarchi, Richard Dennis; Fan, Li; Long, Harlan Beall
PA Lilly, Eli, and Co., USA
SO Eur. Pat. Appl., 15 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07K014-65
ICS A61K038-30
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 3, 63
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 742228	A1	19961113	EP 1996-303134	19960503 <--
	R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
	US 5622932	A	19970422	US 1995-435252	19950505 <--
	JP 08301899	A2	19961119	JP 1996-111473	19960502 <--
	CA 2175786	AA	19961106	CA 1996-2175786	19960503 <--
PRAI	US 1995-435252		19950505 <--		

AB The instant invention provides two-chain **IGF-1** superagonists which are derivs. of the naturally occurring single-chain **IGF-1** having an abbreviated C domain. The invention also provides synthetic and semi-synthetic DNA sequences, recombinant DNA vectors and transformed host cells useful in the recombinant prodn. of these analogs. The invention also provides pharmaceutical formulations comprising these **IGF-1** analogs. The invention also provides methods of using these analogs in a variety of therapeutic applications. The instant invention provides **IGF-1** analogs of the formula: BCn,A (1) wherein: B is the B domain **IGF -1** or a functional analog thereof, C is the C domain of **IGF-1** or a functional analog thereof, n is the no. of amino acids in the C domain and is from about 6 to about 12, and A is the A domain of **IGF-1** or a functional analog thereof.
ST **IGF1** superagonist prepn
IT Anti-AIDS drugs
Antitumor agents
Diabetes mellitus
Diabetic neuropathy
Osteoporosis
Renal failure
Septicemia
(prepn. and formulation of **IGF-1** superagonists for treating a variety of diseases)
IT Growth hormone deficiency
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(prepn. and formulation of **IGF-1** superagonists for treating a variety of diseases)
IT **68562-41-4DP**, Human **IGF-I**, two-chain analogs
185226-61-3P 185226-62-4P 185226-63-5P
RL: **BAC (Biological activity or effector, except adverse)**; SPN (Synthetic preparation); **THU (Therapeutic use)**; BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. and formulation of **IGF-1** superagonists for treating a variety of diseases)
IT 115228-11-0 185226-58-8
RL: RCT (Reactant)

(prepn. and formulation of **IGF-1** superagonists for treating a variety of diseases)

IT 9004-10-8, Insulin, biological studies **61912-98-9, IGF**
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(resistance; prepn. and formulation of **IGF-1** superagonists for treating a variety of diseases)

L53 ANSWER 16 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1997:28476 HCAPLUS
DN 126:70228
TI **Insulin-like growth factor I**: physiology, metabolic effects and **clinical uses**
AU Froesch, E. Rudolf; Hussain, Mehboob A.; Schmid, Christoph; Zapf, Jurgen
CS Division of Endocrinology and Diabetes, Department of Internal Medicine, University Hospital, Zurich, Switz.
SO Diabetes/Metab. Rev. (**1996**), 12(3), 195-215
CODEN: DMREEG; ISSN: 0742-4221
PB Wiley
DT Journal; General Review
LA English
CC 2-0 (Mammalian Hormones)
AB A review, with 117 refs., on **IGF-I** deficiency and receptor defects, role of **IGF-I** in non-insulin-dependent diabetes mellitus and extrapancreatic **tumor** hypoglycemia, metabolic effects of exogenous recombinant human **IGF-I**, growth and anabolic effects of recombinant human **IGF-I**, recombinant human **IGF-I** therapy in diabetes mellitus, and **IGF-I** in osteoporosis.
ST review **IGF**
IT **67763-96-6, IGF-I**
RL: **BAC (Biological activity or effector, except adverse)**; BPR (Biological process); **THU (Therapeutic use)**; BIOL (Biological study); PROC (Process); USES (Uses)
(**insulin-like growth factor I** physiol., metabolic effects, and clin. uses)

L53 ANSWER 17 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1996:251244 HCAPLUS
DN 124:308402
TI The lack of an effect by insulin or **insulin-like growth factor-1** in attenuating colon-26-mediated **cancer cachexia**
AU Lazarus, Douglas D.; Kambayashi, Taku; Lowry, Stephen F.; Strassmann, Gideon
CS Department of Immunology, Otsuka America Pharmaceutical, Inc., Rockville, MD, 20850, USA
SO Cancer Lett. (Shannon, Irel.) (**1996**), 103(1), 71-7
CODEN: CALEDQ; ISSN: 0304-3835
DT Journal
LA English
CC 2-10 (Mammalian Hormones)
Section cross-reference(s): 14
AB In several studies, the anabolic hormones **insulin-like growth factor-1** (**IGF-1**) and insulin attenuated several metabolic changes assocd. with **cancer** cachexia. In the present study, we evaluated the effect of these hormones on the cachexia assocd. with colon-26 (C-26) **tumor**. Healthy age-matched and **tumor**-bearing mice were treated with two daily doses of **IGF-1** (50 .mu.g/kg in toto), or insulin (1 U in toto). Determinants of cachexia were body and **tumor** wt., epididymal fat pad and serum glucose concns. Neither **IGF-1** nor insulin treatment had a significant effect on the cachectic parameters of C-26-bearing mice. These hormones were biol. active, being capable of inducing wt. gain in hypophysectomized mice and

hypoglycemia, resp. Although **IGF-1** and insulin have been used to treat **cancer**-related wt. loss, the research presented here suggests that the beneficial effect of these hormones is not universal.

ST insulin **IGF** colon **cancer** cachexia

IT Adipose tissue
(epididymal; insulin and **IGF-1** effect on colon-26-mediated **cancer** cachexia)

IT Anabolic agents
Blood sugar
Body weight
(insulin and **IGF-1** effect on colon-26-mediated **cancer** cachexia)

IT Cachexia
(**cancerous**, insulin and **IGF-1** effect on colon-26-mediated **cancer** cachexia)

IT Intestine, **neoplasm**
(colon, **adenocarcinoma**, insulin and **IGF-1** effect on colon-26-mediated **cancer** cachexia)

IT 9004-10-8, Insulin, biological studies **67763-96-6, IGF-1**
RL: **BAC (Biological activity or effector, except adverse)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(insulin and **IGF-1** effect on colon-26-mediated **cancer** cachexia)

L53 ANSWER 18 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:916687 HCAPLUS
DN 123:308189
TI **Sensitive cancer** test
IN Hochberg, Abraham; Ariel, Ilana
PA Rapaport, Erich, Israel; Yissum Research Development Co. Hebrew University; Hadasit Medical Research Services and Development Co.
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C12Q001-68
CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 14

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9524503	A1	19950914	WO 1995-EP823	19950306 <--
	W: AU, CA, CZ, FI, HU, JP, KR, MX, NZ, PL, RO, RU, SK, UA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	IL 108879	A1	20000831	IL 1994-108879	19940307 <--
	AU 9518930	A1	19950925	AU 1995-18930	19950306 <--
	EP 759092	A1	19970226	EP 1995-927570	19950306 <--
	R: CH, DE, ES, FR, GB, LI, NL				
	US 5955273	A	19990921	US 1996-704786	19960906 <--
PRAI	IL 1994-108879	A	19940307 <--		
	WO 1995-EP823	W	19950306 <--		

AB A very sensitive assay for the early detection of human **cancer**, of various types is based on the use of a mol. marker, designated as Gene H19, which is used for in situ hybridization of a tissue sample and for indicating the absence or presence of a **malignancy** and its grading by a suitable marker. The probe can be derived from the H19 gene by subcloning at a suitable site in a plasmid, antisense RNA is produced by transcription with a polymerase and suitable fragments are labeled to produce, after hybridization, the desired signal. The label can be radioactive or fluorescent, or a color reagent can be used. Among **malignancies** assayed are a trophoblastic **tumor**, bladder **carcinoma**, ovarian **teratoma**, pediatric Wilms **tumor**, **rhabdomyosarcoma**, and testicular **cancer**. Also a kit for carrying out such an assay is provided.

ST **cancer** diagnosis gene H19 marker hybridization
IT Embryo
Fluorescent substances
Isotope indicators
Kidney
Neoplasm
Plasmid and Episome
Testis, neoplasm
Ureter
(human **cancer** diagnosis using gene H19 as marker and in situ hybridization)
IT Gene, animal
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(H19, human **cancer** diagnosis using gene H19 as marker and in situ hybridization)
IT Kidney, **neoplasm**
(Wilms', human **cancer** diagnosis using gene H19 as marker and in situ hybridization)
IT Ribonucleic acids
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(antisense, human **cancer** diagnosis using gene H19 as marker and in situ hybridization)
IT Embryo
(fetus, human **cancer** diagnosis using gene H19 as marker and in situ hybridization)
IT Chromosome
(human 11, human **cancer** diagnosis using gene H19 as marker and in situ hybridization)
IT Nucleic acid hybridization
(in situ, human **cancer** diagnosis using gene H19 as marker and in situ hybridization)
IT Trophoblast
(**neoplasm**, human **cancer** diagnosis using gene H19 as marker and in situ hybridization)
IT Bladder
(**neoplasm, carcinoma**, human **cancer** diagnosis using gene H19 as marker and in situ hybridization)
IT **Myoma**
(**rhabdomyosarcoma**, human **cancer** diagnosis using gene H19 as marker and in situ hybridization)
IT Ovary, **neoplasm**
(**teratoma**, human **cancer** diagnosis using gene H19 as marker and in situ hybridization)
IT **67763-97-7, IGF2**
RL: ANT (Analyte); **THU (Therapeutic use)**; ANST (Analytical study); BIOL (Biological study); USES (Uses)
(human **cancer** diagnosis using gene H19 as marker and in situ hybridization)

L53 ANSWER 19 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:341048 HCAPLUS
DN 122:114888
TI Compositions and methods for treating **cancer** and **hyperproliferative** disorders
IN Nacy, Carol A.; Holaday, John W.
PA Entremed, Inc., USA
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K039-00
ICS A61K039-12; C07K003-00; C07K013-00; C07K015-00; C07K017-00
CC 63-3 (Pharmaceuticals)

Section cross-reference(s): 2, 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9427635	A1	19941208	WO 1994-US5927	19940526 <--
	W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TT, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	CA 2163652	AA	19941208	CA 1994-2163652	19940526 <--
	AU 9469890	A1	19941220	AU 1994-69890	19940526 <--
	EP 702563	A1	19960327	EP 1994-918667	19940526 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 08510751	T2	19961112	JP 1994-500957	19940526 <--
	US 5919459	A	19990706	US 1995-467101	19950606 <--
PRAI	US 1993-68717		19930527 <--		
	WO 1994-US5927		19940526 <--		
	US 1994-271557		19940707 <--		

AB The present invention encompasses methods for reducing or inhibiting growth factor in **cancer** cells and tissues. More particularly immunogenic growth factor-contg. compns. are administered to a human or animal with a **cancer** or **tumor**. The immunogenic compns. elicit the prodn. of antibodies specific for growth factor which reduce the level or circulating growth factor, thus reducing or eliminating the **proliferation** of **cancer**. The present invention encompasses growth factor-contg. liposomes and vesicles having portions of growth factor externally presented on their surfaces. The present invention also includes antibodies specific for growth factor. Thus, according to the present invention, growth factor levels are reduced either by active immunization of an individual using immunogenic growth factor-contg. compns. or by passive immunization via administering to the individual an antibody or a group of antibodies specific for growth factor.

ST immunogen growth factor **cancer hyperproliferation**

IT Vaccines
(immunogenic growth factor compns. for treating **cancer** and **hyperproliferative** disorders)

IT Animal growth regulators
Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunogenic growth factor compns. for treating **cancer** and **hyperproliferative** disorders)

IT Animal growth regulators
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blood platelet-derived growth factors, immunogenic growth factor compns. for treating **cancer** and **hyperproliferative** disorders)

IT Lymphokines and Cytokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(interleukins, immunogenic growth factor compns. for treating **cancer** and **hyperproliferative** disorders)

IT Glycophospholipids
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lipid A, immunogenic growth factor compns. for treating **cancer** and **hyperproliferative** disorders)

IT Pharmaceutical dosage forms
(liposomes, immunogenic growth factor compns. for treating **cancer** and **hyperproliferative** disorders)

IT Animal growth regulators
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(neuroglia growth factors, immunogenic growth factor compns. for treating **cancer** and **hyperproliferative** disorders)

IT Animal growth regulators
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**schwannoma**-derived growth factors, immunogenic growth factor

compns. for treating **cancer** and **hyperproliferative** disorders)

IT Animal growth regulators
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transforming growth factors, immunogenic growth factor compns. for treating **cancer** and **hyperproliferative** disorders)

IT Lymphokines and Cytokines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**tumor** necrosis factor, immunogenic growth factor compns. for treating **cancer** and **hyperproliferative** disorders)

IT 57-10-3, Palmitic acid, biological studies 57-11-4, Stearic acid, biological studies 60-33-3, Linoleic acid, biological studies 112-80-1, Oleic acid, biological studies 143-07-7, Lauric acid, biological studies 463-40-1, Linolenic acid 544-63-8, Myristic acid, biological studies 7784-30-7, Aluminum phosphate 9002-62-4, Prolactin, biological studies 9061-61-4, Nerve growth factor 21645-51-2, Aluminum hydroxide, biological studies 53678-77-6D, Muramyl dipeptide, derivs. 62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal growth factor 62683-29-8, Colony stimulating factor **67763-96-6, Insulin-like growth factor 1 67763-97-7, Insulin-like growth factor 2** 127464-60-2, Vascular endothelial growth factor 148348-15-6, Fibroblast growth factor 7
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(immunogenic growth factor compns. for treating **cancer** and **hyperproliferative** disorders)

L53 ANSWER 20 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:340980 HCAPLUS
DN 122:97266
TI **Insulin-like growth factor II as antitumor agent**
IN Schofield, Paul; Rees, Robert Charles; Skottner-Lundin, Anna
PA Pharmacia AB, Swed.; Cancer Research Compaing Technology Ltd.
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K037-24
CC 2-10 (Mammalian Hormones)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 9426300	A1	19941124	WO 1994-GB1030	19940512	<--
	W: AU, CA, JP, NZ, US					
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE					
	CA 2162594	AA	19941124	CA 1994-2162594	19940512	<--
	AU 9466547	A1	19941212	AU 1994-66547	19940512	<--
	AU 682862	B2	19971023			
	EP 697885	A1	19960228	EP 1994-915218	19940512	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE					
	JP 08510230	T2	19961029	JP 1994-525163	19940512	<--
	US 5902788	A	19990511	US 1996-549676	19960515	<--
PRAI	GB 1993-10049		19930512	<--		
	WO 1994-GB1030		19940512	<--		

AB **IGF-II** was used for the manuf. of a medicament for the treatment of **tumors**, and esp. for the manuf. of a medicament for growth inhibition of **melanoma** cells and for the treatment of cutaneous melanomas. The medicament could be systematically or locally administered.

ST **insulin like growth factor II antitumor; IGF II melanoma** inhibitor

IT **Neoplasm inhibitors**
(**IGF-II** as)

IT **Neoplasm inhibitors**

(**melanoma, IGF-II** as)
IT **67763-97-7, IGF-II**
RL: **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**melanoma** and **tumor** treatment with)

L53 ANSWER 21 OF 21 HCAPLUS COPYRIGHT 2001 ACS
AN 1995:334467 HCAPLUS
DN 122:96866
TI **Insulin-like growth factor-1** is not **mitogenic** for the Walker-256 **carcinosarcoma**
AU Wan, J. M. F.; Istfan, N. W.; Ye, S. L.; Bistrian, B. R.
CS Dep. Zool., Univ. Hong Kong, Hong Kong
SO Life Sci. (**1995**), 56(10), 747-56
CODEN: LIFSAK; ISSN: 0024-3205
DT Journal
LA English
CC 2-5 (Mammalian Hormones)
AB This study was designed to det. whether i.v. infusion of recombinant human **IGF-1** stimulates **tumor** growth. To det. the potential interaction between nutrition and **IGF-1** administration the study was conducted in fasting rats and during continuous feeding by total parenteral nutrition. **Tumor** cell cycle kinetics including labeling index, DNA synthesis time, cell cycle time in G0/G1, and G2/M in the total cell cycle, and potential doubling time were detd. by flow cytometry after in vivo pulse labeling the rats bearing the Walker-256 **carcinosarcoma** with 5'-bromo-2'-deoxyuridine (BrdUrd). The results show that **IGF-1** treatment has no significant effects on the **proliferative** characteristics of the **tumor** model regardless of the feeding status of the animal. This study provides preliminary cell-cycle kinetics data on the short-term effect of **IGF-1** on **tumor** growth. Failure to show a significant effect of **IGF-1** on the **proliferative** characteristics of the **tumor** suggests that **IGF-1** may be given to **cancer** patients in amts. sufficient to promote wt. gain without deleterious stimulation of **tumor proliferation**.
ST **IGF 1 tumor** growth; **carcinosarcoma** growth **IGF 1**
IT **Neoplasm**
(**IGF-1** is not mitogenic for)
IT Cell cycle
Cell **proliferation**
(**IGF-1** is not mitogenic for Walker-256 **carcinosarcoma**)
IT **Sarcoma**
(**carcino-**, Walker-256; **IGF-1** is not mitogenic for)
IT **67763-96-6, IGF-1**
RL: **BAC (Biological activity or effector, except adverse)**; **THU (Therapeutic use)**; BIOL (Biological study); USES (Uses)
(**IGF-1** is not mitogenic for Walker-256 **carcinosarcoma**)

=> fil medline
FILE 'MEDLINE' ENTERED AT 11:46:49 ON 18 SEP 2001

FILE LAST UPDATED: 17 SEP 2001 (20010917/UP). FILE COVERS 1958 TO DATE.

On April 22, 2001, MEDLINE was reloaded. See HELP RLOAD for details.

MEDLINE now contains IN-PROCESS records. See HELP CONTENT for details.

MEDLINE is now updated 4 times per week. A new current-awareness alert frequency (EVERYUPDATE) is available. See HELP UPDATE for more information.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2001 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

=> d all 16 18 19 23 24 26 27

L67 ANSWER 16 OF 27 MEDLINE
AN 93274860 MEDLINE
DN 93274860 PubMed ID: 8501905
TI Effect of **insulin-like growth factor 1** on host response to tumor.
AU Dong Y L; Fleming R Y; Huang K F; Herndon D N; Yan T Z; Waymack J P
CS Shriners Burns Institute, Galveston-Unit, Texas 77550-2750.
NC GM08256-03 (NIGMS)
SO JOURNAL OF SURGICAL ONCOLOGY, **(1993 Jun)** 53 (2) 121-7.
Journal code: K79; 0222643. ISSN: 0022-4790.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199306
ED Entered STN: 19930716
Last Updated on STN: 19930716
Entered Medline: 19930630
AB Oncology patients suffer multiple detrimental metabolic alterations. Among these are catabolism of tumor free body mass to supply nutrients to feed the tumor. This results not only in enhanced tumor growth but also poor wound healing and immunosuppression of the tumor host. Efforts are therefore being directed at finding methods for improving the nutritional status of the tumor host without enhancing tumor growth. We investigated the ability of two hormones, **insulin-like growth factor-1** (**IGF-1**) and insulin, to improve physiologic function in tumor-bearing animals. Tumor-bearing animals received a continuous infusion of **IGF-1** (2.20 mg/kg/day), insulin (820 microns/kg/day) or placebo via an osmotic minipump for 7 days. All animals were pair fed to eliminate nutritional intake as a variable. The placebo group lost 31.37 +/- 4.3 g of tumor free body mass during the study period. The insulin treated group lost 26.34 +/- 7.42 g and the **IGF-1** group lost 5.07 +/- 3.25 g ($P < 0.001$, ANOVA). **IGF-1** treatment failed to alter plasma glucose, lactate, or total amino acid concentration and failed to alter hepatic ketone body concentrations, but did improve hepatic mitochondria redox potential. Finally, **IGF-1** improved splenic weight by 110% and splenic lymphocyte count by 300%. In conclusion **IGF-1** appears to offer potential in supporting tumor free host body mass without stimulating tumor growth.
CT Check Tags: Animal; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Amino Acids: DE, drug effects
Analysis of Variance
***Colonic Neoplasms: DT, drug therapy**
Colonic Neoplasms: PP, physiopathology
*Insulin: TU, therapeutic use
***Insulin-Like Growth Factor I: TU, therapeutic use**
Lymphocyte Transformation: DE, drug effects
Mitosis: DE, drug effects
Random Allocation
Rats

Rats, Inbred WF
Recombinant Proteins: TU, therapeutic use
RN 11061-68-0 (Insulin); **67763-96-6 (Insulin-Like Growth Factor I)**
CN 0 (Amino Acids); 0 (Recombinant Proteins)

L67 ANSWER 18 OF 27 MEDLINE
AN 93155591 MEDLINE
DN 93155591 PubMed ID: 8429272
TI Comparison of the effects of **insulin-like growth factors-I** and -II on the human osteosarcoma cell line OHS-4.
AU Fournier B; Ferralli J M; Price P A; Schlaeppi J M
CS Pharmaceuticals Research Laboratories, CIBA-GEIGY Ltd, Basel, Switzerland.
SO JOURNAL OF ENDOCRINOLOGY, **(1993 Jan)** 136 (1) 173-80.
Journal code: I1J; 0375363. ISSN: 0022-0795.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199303
ED Entered STN: 19930326
Last Updated on STN: 19980206
Entered Medline: 19930308
AB The effects of **insulin-like growth factor-I** (**IGF-I**) and **IGF-II** on the human osteoblast cell-line OHS-4 were investigated. Both **IGF-I** and **IGF-II** stimulated cell proliferation at nanomolar concentrations and alkaline phosphatase activity was decreased in a dose-dependent manner with either **IGF-I** or **IGF-II**. The production of the bone-specific protein osteocalcin was not influenced by either **IGF-I** or **IGF-II**. However, they acted synergistically with 1,25-dihydroxy-vitamin D3 at concentrations ranging from 10 to 100 nmol/l. Neither **IGF-I** nor **IGF-II** had an effect on either the basal or the parathyroid hormone-stimulated level of adenylate cyclase activity, and likewise they had no effect on phosphodiesterase activity. Binding and cross-linking experiments confirmed the presence of both type-I and type-II **IGF** receptors on the OHS-4 cells. The present study shows that **IGF-I** and **IGF-II** have similar effects on the parameters studied in these osteoblastic cells. They influenced both proliferation and differentiation markers.
CT Check Tags: Comparative Study; Human
Adenylate Cyclase: ME, metabolism
Alkaline Phosphatase: ME, metabolism
Cell Differentiation: DE, drug effects
Cell Division: DE, drug effects
Cell Line
Dose-Response Relationship, Drug
***Insulin-Like Growth Factor I: PD, pharmacology**
***Insulin-Like Growth Factor II: PD, pharmacology**
Osteoblasts: DE, drug effects
Osteoblasts: EN, enzymology
***Osteosarcoma: DT, drug therapy**
Osteosarcoma: EN, enzymology
Parathyroid Hormones: PD, pharmacology
Receptors, Somatomedin: ME, metabolism
RN **67763-96-6 (Insulin-Like Growth Factor I); 67763-97-7 (Insulin-Like Growth Factor II)**
CN 0 (Parathyroid Hormones); 0 (Receptors, Somatomedin); EC 3.1.3.1 (Alkaline Phosphatase); EC 4.6.1.1 (Adenylate Cyclase)

L67 ANSWER 19 OF 27 MEDLINE
AN 92399166 MEDLINE
DN 92399166 PubMed ID: 1355995
TI Polypeptide growth factors: their potential value in the management of

breast cancer patients.
AU Osborne C K
NC P01 CA30195 (NCI)
R01 CA30251 (NCI)
SO CANCER TREATMENT AND RESEARCH, **(1992)** 60 315-29. Ref: 50
Journal code: AVA; 8008541. ISSN: 0927-3042.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199210
ED Entered STN: 19921106
Last Updated on STN: 19950206
Entered Medline: 19921022
CT Check Tags: Female; Human; Support, U.S. Gov't, P.H.S.
Antibodies, Monoclonal: TU, therapeutic use
***Breast Neoplasms: DT, drug therapy**
*Growth Substances: PH, physiology
Insulin-Like Growth Factor I: PD, pharmacology
Insulin-Like Growth Factor II: PD, pharmacology
Prognosis
Receptors, Cell Surface: PH, physiology
Receptors, Somatomedin
Transforming Growth Factor alpha: AN, analysis
Transforming Growth Factor beta: PD, pharmacology
Transforming Growth Factor beta: TU, therapeutic use
RN **67763-96-6 (Insulin-Like Growth Factor I); 67763-97-7 (Insulin-Like Growth Factor II)**
CN 0 (Antibodies, Monoclonal); 0 (Growth Substances); 0 (Receptors, Cell Surface); 0 (Receptors, Somatomedin); 0 (Transforming Growth Factor alpha); 0 (Transforming Growth Factor beta)

L67 ANSWER 23 OF 27 MEDLINE
AN 92118397 MEDLINE
DN 92118397 PubMed ID: 1722685
TI **IGF-I** and **IGF**-binding proteins: stimulatory and inhibitory factors secreted by human prostatic adenocarcinoma cells.
AU Kaicer E K; Blat C; Harel L
CS Institut de Recherches Scientifiques sur le Cancer, Villejuif, France.
SO GROWTH FACTORS, **(1991)** 4 (3) 231-7.
Journal code: AOI; 9000468. ISSN: 0897-7194.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199202
ED Entered STN: 19920315
Last Updated on STN: 19970203
Entered Medline: 19920224
AB Deregulation of growth observed in malignant cell cultures has been assumed to be the result of increased secretion by these cells of autocrine growth factors, as well as the decreased sensitivity of these cells to inhibitory molecules which are diffused from normal or transformed cells. Our results show that PC-3 cells secreted into the medium, factors having stimulatory and inhibitory activities. We found an **IGF**-like molecule in medium conditioned by PC-3 cells. Its concentration was less than 1 ng/ml of conditioned medium. We demonstrated that PC-3 cells have receptors for **IGF-I** and are stimulated by this growth factor. However, the dose response curve shows that 1 ng/ml of **IGF-I** is not sufficient to indicate autocrine growth regulation by **IGF** of prostatic carcinoma cells. **IGF**-binding proteins of 90,000, 45,000, 34,000 and 28,000 molecular weight were also secreted by PC-3 cells. It is noteworthy that the secreted proteins which had the greatest inhibitory effect on chick

embryo fibroblast growth also has the strongest **IGF**-binding activity. The probability that the **IGF**-binding protein secreted by PC-3 cells inhibited serum stimulation of DNA synthesis by preventing stimulation induced by **IGF** present in the serum is discussed. It is of interest that these **IGF**-binding proteins inhibited chick embryo fibroblast proliferation but did not inhibit PC-3 cells. This is in agreement with the assumption that **IGF** present in the medium is not an autocrine growth factor for these cells.

CT Check Tags: Animal; Human; Male; Support, Non-U.S. Gov't
Adenocarcinoma: DT, drug therapy
***Adenocarcinoma: SE, secretion**
Carrier Proteins: PD, pharmacology
*Carrier Proteins: SE, secretion
Cell Line
Chick Embryo
Culture Media
Fibroblasts: DE, drug effects
Fibroblasts: PH, physiology
Insulin-Like Growth Factor I: PD, pharmacology
***Insulin-Like Growth Factor I: SE, secretion**
Insulin-Like Growth-Factor-Binding Proteins
Molecular Weight
Prostatic Neoplasms: DT, drug therapy
***Prostatic Neoplasms: SE, secretion**
Receptors, Cell Surface: DE, drug effects
Receptors, Cell Surface: ME, metabolism
Receptors, Somatomedin
Somatomedins: ME, metabolism
Tumor Cells, Cultured

RN **67763-96-6 (Insulin-Like Growth Factor I)**

CN 0 (Carrier Proteins); 0 (Culture Media); 0 (**Insulin-Like Growth-Factor**-Binding Proteins); 0 (Receptors, Cell Surface); 0 (Receptors, Somatomedin); 0 (Somatomedins)

L67 ANSWER 24 OF 27 MEDLINE

AN 92093799 MEDLINE

DN 92093799 PubMed ID: 1661415

TI Mitogenic effects of insulin and **insulin-like growth factors** on PA-III rat prostate adenocarcinoma cells: characterization of the receptors involved.

AU Polychronakos C; Janthly U; Lehoux J G; Koutsilieris M

CS Polypeptide Hormone Laboratory, McGill University, Montreal, Quebec, Canada.

SO PROSTATE, **(1991)** 19 (4) 313-21.
Journal code: PB4; 8101368. ISSN: 0270-4137.

CY United States

DT Journal; Article; (JOURNAL ARTICLE)

LA English

FS Priority Journals

EM 199201

ED Entered STN: 19920216
Last Updated on STN: 20000303
Entered Medline: 19920124

AB Four transplantable cell lines (PA-I, II, III, and IV) derived from four Lobund-Wistar (L-W) rats that manifested spontaneous prostate cancer have demonstrated metastatic capacity in visceral organs. Interestingly, PA-III cells, when deposited over the scapula or calvarium of the Lobund-Wistar rat, could produce lytic and blastic reactions on rat skeleton. Since growth factors and growth factor receptors have been implicated in bone remodeling, cancer biology, and metastatic growth of cancer cells, we have examined 1) the effects of insulin and **insulin-like growth factors** (**IGF-I** and **IGF-II**) on the proliferation of PA-III cells; and 2) the presence of specific receptors for these peptides. **IGF-I** (0.5 to 100 ng/ml), **IGF-II** (0.5 to 100 ng/ml), and insulin (0.5 to 10 micrograms/ml) stimulated tritiated thymidine uptake

and increased the number of PA-III cells in culture. Receptor studies demonstrated the presence of specific bindings sites for **IGF-I** and II but not for insulin. The number and affinity of the receptor sites were: **IGF-I** (nb = 675 fmol/100 g protein, Kd = 0.56 nmol) and **IGF-II** (nb = 225 fmol/100 g protein, Kd = 0.71 nmol). Molecular characterization of **IGF** binding sites by polyacrylamide gel electrophoresis under denaturing conditions indicated only the presence for the type I **IGF** receptor. The presence of the **IGF-I** receptor and the absence of **IGF-II** and insulin receptors are discussed in relation to the capacity of PA-III cells to produce bone lesions on the L-W rat.

CT Check Tags: Animal; Male; Support, Non-U.S. Gov't
Adenocarcinoma: DT, drug therapy
Adenocarcinoma: PA, pathology
***Adenocarcinoma: UL, ultrastructure**
Cell Division: DE, drug effects
Insulin: ME, metabolism
*Insulin: PD, pharmacology
Insulin-Like Growth Factor I: ME, metabolism
***Insulin-Like Growth Factor I: PD, pharmacology**
Insulin-Like Growth Factor II: ME, metabolism
***Insulin-Like Growth Factor II: PD, pharmacology**
Kinetics
Membranes: ME, metabolism
Mitogens: PD, pharmacology
Prostatic Neoplasms: DT, drug therapy
Prostatic Neoplasms: PA, pathology
***Prostatic Neoplasms: UL, ultrastructure**
Rats
Receptor, Insulin: ME, metabolism
*Receptor, Insulin: PH, physiology
Receptors, Cell Surface: ME, metabolism
*Receptors, Cell Surface: PH, physiology
Receptors, Somatomedin

RN 11061-68-0 (Insulin); **67763-96-6 (Insulin-Like Growth Factor I); 67763-97-7 (Insulin-Like Growth Factor II)**

CN 0 (Mitogens); 0 (Receptors, Cell Surface); 0 (Receptors, Somatomedin); EC 2.7.11.- (Receptor, Insulin)

L67 ANSWER 26 OF 27 MEDLINE
AN 91137105 MEDLINE
DN 91137105 PubMed ID: 2178363
TI Regulation of breast cancer growth by **insulin-like growth factors.**
AU Osborne C K; Clemmons D R; Arteaga C L
CS Department of Medicine, University of Texas Health Science Center, San Antonio 78284-7884.
NC AG 02331 (NIA)
PO1 30195
SO JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, **(1990 Dec 20)** 37 (6) 805-9.
Journal code: AX4; 9015483. ISSN: 0960-0760.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199103
ED Entered STN: 19910412
Last Updated on STN: 19970203
Entered Medline: 19910327
AB The **IGFs** may be important autocrine, paracrine or endocrine growth factors for human breast cancer. **IGF-I** and II stimulate growth of cultured human breast cancer cells. **IGF-I** is slightly more potent, paralleling its higher affinity for the **IGF-I** receptor. Antibody blockade of the **IGF-**

I receptor inhibits growth stimulation induced by both **IGFs**, suggesting that this receptor mediates the growth effects of both peptides. However, **IGF-I** receptor blockade does not inhibit estrogen (E2)-induced growth suggesting that secreted **IGFs** are not the major mediators of E2 action. Several breast cancer cell lines express **IGF-II** mRNA by both Northern analysis and RNase protection assay. **IGF-II** activity is found in conditioned medium by radioimmuno and radioreceptor assay, after removal of somatomedin binding proteins (BP) which are secreted in abundance. **IGF-I** is undetectable. BPs of congruent to 25 and 40 K predominate in ER-negative cell lines while BPs of 36 K predominate in ER-positive cells. Blockade of the **IGF-I** receptor inhibits anchorage-independent and monolayer growth in serum of a panel of breast cancer cell lines. Growth of one line (MDA-231) was also inhibited in vivo by receptor antibody treatment of nude mice. The antibody had no effect on growth of MCF-7 tumors. These data suggest that **IGFs** are important regulators of breast cancer cell proliferation and that antagonism of this pathway may offer a new treatment strategy.

CT Check Tags: Human; Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
*Antineoplastic Agents: PD, pharmacology
***Breast Neoplasms: DT, drug therapy**
Estrogens: PD, pharmacology
***Insulin-Like Growth Factor I: PD, pharmacology**
***Insulin-Like Growth Factor II: PD, pharmacology**
Receptors, Cell Surface: ME, metabolism
Receptors, Somatomedin
Tumor Cells, Cultured

RN **67763-96-6 (Insulin-Like Growth Factor I); 67763-97-7 (Insulin-Like Growth Factor II)**

CN 0 (Antineoplastic Agents); 0 (Estrogens); 0 (Receptors, Cell Surface); 0 (Receptors, Somatomedin)

L67 ANSWER 27 OF 27 MEDLINE
AN 91113513 MEDLINE
DN 91113513 PubMed ID: 1846553
TI Co-stimulation of gastrointestinal tumour cell growth by gastrin, transforming growth factor alpha and **insulin like growth factor-I.**
AU Durrant L G; Watson S A; Hall A; Morris D L
CS Cancer Research Campaign Laboratories, University of Nottingham, UK.
SO BRITISH JOURNAL OF CANCER, **(1991 Jan)** 63 (1) 67-70.
Journal code: AV4; 0370635. ISSN: 0007-0920.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199103
ED Entered STN: 19910329
Last Updated on STN: 20000303
Entered Medline: 19910306

AB Epidermal growth factor receptors and **insulin like growth factor-I** receptors were co-expressed on two gastric and three colorectal tumour cell lines. Previous studies have shown that gastrin receptors were also expressed at a low level or two of these cell lines. Both TGF alpha and **IGF-I** promoted cell growth in all of the cell lines tested. The cell doubling time of a colorectal cell line was reduced from 48 to 30-34 h. Furthermore the effects of the growth factors were additive. Each growth factor also increased the response of the cells to gastrin, but a combination of both growth factors and gastrin did not further increase growth.

CT Check Tags: Human
Cell Division: DE, drug effects
Colonic Neoplasms: DT, drug therapy
***Colonic Neoplasms: PA, pathology**
Colonic Neoplasms: UL, ultrastructure

Drug Synergism
Drug Therapy, Combination
*Gastrins: PD, pharmacology
***Insulin-Like Growth Factor I: PD, pharmacology**
Mitogens: PD, pharmacology
Receptor, Epidermal Growth Factor: PH, physiology
Receptors, Cell Surface: PH, physiology
Receptors, Somatomedin
Stomach Neoplasms: DT, drug therapy
***Stomach Neoplasms: PA, pathology**
Stomach Neoplasms: UL, ultrastructure
*Transforming Growth Factor alpha: PD, pharmacology
Tumor Cells, Cultured
RN **67763-96-6 (Insulin-Like Growth Factor I)**
CN 0 (Gastrins); 0 (Mitogens); 0 (Receptors, Cell Surface); 0 (Receptors, Somatomedin); 0 (Transforming Growth Factor alpha); EC 2.7.11.- (Receptor, Epidermal Growth Factor)

=> d his

(FILE 'HOME' ENTERED AT 10:25:50 ON 18 SEP 2001)
SET COST OFF

FILE 'REGISTRY' ENTERED AT 10:25:59 ON 18 SEP 2001
L1 118 S GPETLCGAELVDALQFVCGDRGF.FNKPTG.GSSSRRAPQTGIVDECC...C.L..LEM.C
SAV L1 MOEZIE399/A
L2 42 S L1 AND 70/SQL
E INSULIN-LIKE GROWTH FACTOR/CN
L3 1 S E1
L4 1 S E6
L5 1 S E11
L6 1 S E26
L7 42 S L2 NOT L3-L6
L8 3 S L3-L6
E INSULIN-LIKE GROWTH FACTOR I (HUMAN)/CN
L9 1 S E3
E INSULIN-LIKE GROWTH FACTOR (HUMAN)/CN
E INSULIN-LIKE GROWTH FACTOR II (HUMAN)/CN
L10 1 S E3
L11 5 S L8-L10
L12 4 S L11 NOT L7

FILE 'HCAPLUS' ENTERED AT 10:32:27 ON 18 SEP 2001
L13 162 S L7
L14 16081 S L12
L15 16437 S (IGF OR INSULIN LIKE GROWTH FACTOR OR INSULIN GROWTH FACTOR O
L16 20977 S IGF OR INSULIN LIKE GROWTH FACTOR OR INSULIN GROWTH FACTOR OR
L17 1737 S IGF1 OR IGF2
L18 467 S INSULINLIKE GROWTH FACTOR()(1 OR I OR 2 OR II)
L19 2656 S INSULINLIKE GROWTH FACTOR
L20 5078 S (IGF OR INSULIN LIKE GROWTH FACTOR OR INSULIN GROWTH FACTOR O
L21 763 S SOMATOMEDIN# C
L22 870 S IGFI OR IGFII
L23 21794 S L14-L22
L24 140 S L13 AND (PD<=19981002 OR PRD<=19981002 OR AD<=19981002 OR PY<
L25 16524 S L23 AND (PD<=19981002 OR PRD<=19981002 OR AD<=19981002 OR PY<
E MASCARENHAS D/AU
L26 42 S E3-E6,E10
L27 2 S L26 AND L13
L28 19 S L26 AND L23
L29 2 S L27 AND L25
L30 2 S L27,L29
L31 23 S L7 (L) THU/RL
L32 17 S L31 AND L24
L33 18 S L24 AND (?NEOPLAS? OR ?TUMOR? OR ?TUMOUR? OR ?MALIGNA? OR ?CA

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                E CANCER/CT
                E E3+ALL
                E E2+ALL
L34        193090 S E3-E8,E2+NT
                E E132+ALL
L35         77037 S E4
L36         52430 S E3,E21-E66
                E E68+ALL
L37          3932 S E4,E3
                E HYBRIDOMA/CT
                E E3+ALL
L38          4007 S E6,E5+NT
L39             5 S L24 AND L34-L38
L40            18 S L33,L39
L41             3 S L31 AND L40
L42             5 S L7(L) BAC/RL AND L40
L43             7 S L30,L41,L42
L44             7 S L43 AND L13-L42
                SEL DN 3 6 7
L45             4 S L44 NOT E1-E3
L46          1197 S L25 AND L34-L38
L47          4721 S L25 AND (?NEOPLAS? OR ?TUMOR? OR ?TUMOUR? OR ?MALIGNA? OR ?CA
L48          1109 S L12 (L) THU/RL
L49          4359 S L12 (L) BAC/RL
L50          1129 S L46,L47 AND L48,L49
L51           203 S L12 (L) THU/RL AND L50
L52            18 S L51 AND (ANTITUMOR AGENT OR REDUCE C JUN EXPRESSION OR CACHEX
L53            21 S L45,L52
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 11:34:15 ON 18 SEP 2001
L54             5 S E4-E8

     FILE 'HCAPLUS' ENTERED AT 11:34:31 ON 18 SEP 2001
L55            34 S L31-L33 NOT L53
L56             5 S L55 AND (SYRUP OR BLAST OR MYOBLAST)

     FILE 'REGISTRY' ENTERED AT 11:38:48 ON 18 SEP 2001

     FILE 'REGISTRY' ENTERED AT 11:39:10 ON 18 SEP 2001

     FILE 'HCAPLUS' ENTERED AT 11:39:23 ON 18 SEP 2001

     FILE 'MEDLINE' ENTERED AT 11:40:24 ON 18 SEP 2001
L57            20 S L2
L58         15207 S L12
                E INSULIN-LIKE GROWTH FACTOR/CT
                E E26+ALL
L59         13661 S E38+NT
                E INSULIN-LIKE GROWTH FACTOR/CN
L60         13661 S E8
                E INSULIN LIKE GROWTH FACTOR/CN
L61         22851 S L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22
L62         17713 S L57-L61 AND PY<=1998
L63          2929 S L62 AND C4./CT
L64           284 S L62 AND (C4.(L)DT)/CT
L65          4415 S ((INSULIN-LIKE GROWTH FACTOR I)(L)(TU OR AD OR PD))/CT
L66            27 S L64 AND L65
L67            27 S L63 AND L66

     FILE 'MEDLINE' ENTERED AT 11:46:49 ON 18 SEP 2001
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